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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/849,969	05/08/2001	Randolph J. Noelle	037003-0280613	1327

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/849,969	NOELLE ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-10 and 12-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-10 and 12-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission, filed on 8/26/04, has been entered.

Applicant's amendment, filed 8/26/04, has been entered.
Claims 1 and 12 have been amended.
Claim 21 has been added.

Claims 1, 4-10 and 12-21 are pending and being acted upon presently.

Claims 2, 3 and 11 have been canceled previously.

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1, 4 - 10 and 21 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed:
"wherein the tissue destruction results from a cell-mediated immune reaction to one or more autoantigens".

Applicant's amendment, filed 8/26/04, directs support to pages 3-4 of the instant specification for this "phrase"

However, there does not appear to be sufficient written description for to "one or more autoantigens".

Also, there does not appear to be sufficient written description for "cell-mediated" rather than "T-cell mediated".

The specification as filed does not provide a sufficient written description of specific "limitations" within this newly submitted phrase. The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed.

Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action
Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06

4. Claims 1, 4-10, and 12-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs or biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental evidence accurately reflects the relative ability of gp39-specific antibodies to prevent T cell mediated tissue destruction / autoimmune response associated with type I diabetes, as it reads on preventing type I diabetes.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

Also, it is noted that experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus / insult occur at the same or nearly the same time. Immunosuppression is much easier to achieve under such controlled conditions that experienced in the human immunoregulatory diseases such as "type I diabetes" targeted by the claimed invention. With respect to in vivo studies, animal models validate concepts based on studies of human disease, such studies are limited to the "acute" as opposed to "chronic" nature of the disease. In animal models, the onset of inflammation is rapid with an aggressive destructive process, whereas in humans the disease progresses more slowly, often with natural periods of disease exacerbation and remission. Generally, such diseases are diagnosed only after significant tissue damage has occurred.

In reviewing Prediction and Prevention of Type I Diabetes (Acta Paediatr Suppl 435: 54-62, 1998) (provided as an Exhibit by applicant), Knip describes the limitations of identifying individuals at risk for clinical disease and that there is no effective preventive modality available (see entire document, including the Abstract). In discussing Practical Implications, Knip discloses that of none of the screening tools for type I diabetes provide for the high sensitivity and specificity necessary to establish a positive predictive value (see page 56, column 2, paragraph 2). In the Conclusion, Knip notes that: "The route towards effective prevention of type I diabetes will hardly be a well-paved highway, but rather a path lined by both success and disappointment."

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective prevention of type I diabetes by antibody-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for the relative ability of gp39-specific antibodies to prevent T cell mediated tissue destruction / T cell autoimmune response associated with type I diabetes, as it reads on preventing type I diabetes.

Alternatively, if the claims are intended to read on preventing the elaboration of T cell mediated tissue destruction / autoimmune response associated with type I diabetes as part of a therapeutic regimen during the treatment of type I diabetes rather than preventing type I diabetes per se, then this rejection will be withdrawn.

5. Claim 8 and 21-21 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 8 and 12-20 are indefinite in "or an antibody having the gp39 binding characteristics thereof" does not appear to have proper antecedent basis.

For example, claim 1 appears to be limited to the specific monoclonal anti-gp39 antibodies 89-76 and 24-31 and does not broadly encompass "an antibody having the gp39 binding characteristics thereof".

Also, it is noted that claims 9-10 recite "chimeric" and "humanized" antibodies, again while claim 1 appears to be limited to the specific monoclonal anti-gp39 antibodies 89-76 and 24-31 and does not encompass modifications of said specific monoclonal antibodies.

Alternatively, claim 8 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Rather, it appears to broaden the claim antibody specificities employed in the claimed methods.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

B) Claims 8 and 12-20 are indefinite in the recitation of "binding characteristics" in that the nature or parameters of said "binding characteristics" other than binding to gp39 are ill-defined and ambiguous.

Given that the claims recites the plural "characteristics" rather than simply "binding to gp39", applicant is invited to amend the claims to recite the appropriate binding characteristics contemplated by the metes and bounds of the antibody specificity employed in the claimed methods.

C) Claims 12-20 are indefinite in the recitation of "T cell mediated autoimmune responses associated with type I diabetes" in that the nature or parameters of said "autoimmune responses are ill-defined and ambiguous.

Applicant is invited to amend the claims to recite specific endpoints that can be measured.

D) Claims 12-20 are indefinite in the recitation of "24-31" and "89-76" because their characteristics are not known. The use of "24-31" and "89-76" monoclonal antibodies as the sole means of identifying the claimed antibodies and hybridomas renders the claim indefinite because "24-31" and "89-76"" are merely laboratory designations which does not clearly define the claimed products, since different laboratories may use the same laboratory designation s to define completely distinct hybridomas / cell lines.

While it is noted that independent claim 1 has recited the appropriate ATCC Accession Numbers, claim 12 has been amended to read as an independent claim and the first independent claim, at least should recite the appropriate deposit information for clarity.

E) Claim 21 is indefinite in that it is a method that depends on a method. Furthermore, the claim does not provide additional discrete steps or ingredients to carry out the method.

F) Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. For examination purposes, the claims can be read on preventing the elaboration of T cell mediated tissue destruction / autoimmune responses associated with type I diabetes as part of a therapeutic regimen during the treatment of type I diabetes rather than being limited to preventing type I diabetes per se.

8. Upon reconsideration of applicant's amended claims and arguments, filed 8/26/04, the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Noelle et al. (U.S. Patent No. 5,683,693) has been withdrawn.

9. Given an updated search and consideration that the instant claims are drawn to methods of treating diabetes with gp39-specific / CD40L-specific antibodies, the previous Lederman et al. (U.S. Patent No. 5,993,816) prior art reference has been replaced with Lederman et al. (U.S. Patent No. 6,592,868).

10. Given that claim 1 has been amended to recited the specific 89-76 and 24-31 gp39-specific antibodies, the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Lederman et al. has been withdrawn.

However, it is noted that claim 6 does recite "or an antibody having the gp39 binding characteristics thereof", which has been addressed with a rejection under 35 U.S.C. § 112, second paragraph, above.

If the intent of applicant is encompass gp39-sepcific antibodies other than the specific 89-76 and 24-31 gp39-specific antibodies, such claims would be subject to rejection under 35 U.S.C. § 102(e) as being anticipated by Lederman et al.

11. Claim 12 is rejected under 35 U.S.C. § 102(e) as being anticipated by Lederman et al. (U.S. Patent No. 6,592,868) (see entire document, including Claim 7) for the reasons of record.

Applicant's arguments in conjunction with Exhibits A-C, filed 8/26/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that the skilled artisan at the time the invention would not have found the Lederman patent's claims for preventing tissue-mediated destruction in an autoimmune disease, such as those listed (e.g. rheumatoid arthritis, Myasthenia gravis, SLE, Grave's disease, ITP, hemolytic anemia, diabetes mellitus and drug-induced lupus) credible.

Applicant provides Exhibits A-C to indicated that Lederman's humanized 5c8 antibody failed in a clinical setting of a transplantation therapeutic regimen, while the presently claimed antibody IDEC-131/E6040, which targets a different epitope than Lederman's hu5c8 antibody in autoimmune disease and is safe and well-tolerated.

Applicant is reminded that each claim of a patent (whether in independent, dependent or multiple dependent form) shall be presumed valid. See 35 USC 282.

While applicant provides various Abstracts in Exhibit D to indicate that Lederman's 5c8 antibody would be useful to prevent T cell mediated B cell antibody production and not T cell mediated tissue destruction, there appears to be no manipulative difference between the prior art methods and the claimed methods.

Furthermore, products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Although the reference is silent about the prevention of a T cell mediated autoimmune response associated with type I diabetes, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See MPEP 2145.

In contrast to applicant's assertions and as pointed out previously, Lederman et al. teach the use of 5C8-specific / CD40L-specific antibodies, including chimeric and humanized antibodies (see columns 7-8) to treat autoimmune diseases including diabetes (see column 11, paragraph 5, including Claim 7). Given the inhibitory properties of such 5C8-specific / CD40L-specific antibodies, the prior art teach antibodies having the gp39 binding characteristics of the claimed 89-76 and 24-31 antibodies.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods to treat Type I diabetes with of 5C8-specific / CD40L-specific antibodies.

It does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001).

As indicated above, the claims appear to on preventing a T cell mediated autoimmune response associated with type I diabetes as part of a therapeutic regimen during the treatment of type I diabetes rather than preventing type I diabetes per se, then this rejection will be withdrawn

Applicant's arguments are not found persuasive.

11. Claims 1, 4 –10 and 12 - 21 are rejected under 35 U.S.C. § 103(a) as being unpatentable Lederman et al. (U.S. Patent No. 6,592,868) in view of Noelle et al. (U.S. Patent No. 5,747,037) for the reasons of record.

Applicant's arguments have been fully considered but are not found convincing essentially for the reasons of record.

Applicant argues that Noelle et al. would not have inhibit or prevented tissue destruction from a cell-mediated reaction to self-antigens and does not suggest modification of this method to obtain such a method.

Applicant argues that Lederman fails to the missing teaching since Lederman does not teach T cell mediated tissue destruction but only T cell mediated B cell activation.

Applicant submits that IDDM is a T cell mediated disorder and that the protective effect conferred by transplanting donor spleen cells from animals immunized with PLP-peptides in the EAE animal model of T cell mediated autoimmunity was due to the suppression of the activated T cells.

Applicant also asserts that neither Noelle nor Lederman disclose preventing T cell destruction.

Although Lederman is silent about the prevention of a T cell mediated autoimmune response associated with type I diabetes, it does not appear that the claim language or limitations result in a manipulative difference in the method steps when compared to the prior art disclosure. See Bristol-Myers Squibb Company v. Ben Venue Laboratories 58 USPQ2d 1508 (CAFC 2001). "{i}t is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable." In re Woodruff, 16 USPQ2d 1934, 1936 (Fed. Cir. 1990). The mechanism of action does not have a bearing on the patentability of the invention if the invention was already known or obvious. Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. In re Wiseman, 201 USPQ 658 (CCPA 1979). Granting a patent on the discovery of an unknown but inherent function would remove from the public that which is in the public domain by virtue of its inclusion in, or obviousness from, the prior art. In re Baxter Travenol Labs, 21 USPQ2d 1281 (Fed. Cir. 1991). See M.P.E.P. 2145.

As indicated above, the claims appear to on preventing a T cell mediated tissue destruction / autoimmune response associated with type I diabetes as part of a therapeutic regimen during the treatment of type I diabetes rather than preventing type I diabetes per se, then this rejection will be withdrawn

In contrast to applicant's assertions and as pointed out previously, Lederman et al. teach the use of 5C8-specific / CD40L-specific antibodies, including chimeric and humanized antibodies (see columns 7-8) to treat autoimmune diseases including diabetes (see column 11, paragraph 5, including Claim 7). Further, it is noted that Lederman et al. also teach the applicability of 5c8-specific antibodies to inhibit transplant rejection, a well-known cell mediated immune response. Given the inhibitory properties of such 5C8-specific / CD40L-specific antibodies, the prior art teach antibodies having the gp39 binding characteristics of the claimed 89-76 and 24-31 antibodies. I

As pointed out previously, Noelle et al. ('037) teach the particular 24-31 and 89-76 CD40L-specific antibodies encompassed by the claimed methods, including recombinant forms thereof as well as their use as therapeutic antagonists in inhibiting various immune responses (see entire document, including Detailed Description of the Invention). Noelle et al. teach the methods of their invention can be applied to induce T cell tolerance to a variety of antigens, including antigens involved in autoimmune diseases (see Used of the Method of the Invention on column 13).

Given the antagonistic properties of the particular 24-31 and 89-76 CD40L-specific antibodies taught by Noelle et al. ('037), the ordinary artisan would have been motivated to substitute these CD40L antagonists into the methods of treating autoimmune diseases such as diabetes, as taught by Lederman, given their inhibitory properties were consistent with the antagonistic CD40L-specific antibodies taught by the prior art. Noelle et al. ('037) and Lederman et al. all teach the advantages of anti-CD40L antibodies to inhibit immune responses by targeting the CD40L on T helper cells in therapeutic modalities of immunosuppression at the time the invention was made. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

12. No claim allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
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